## REMARKS/ARGUMENTS

Prior to the present amendments, claims 58-70 were pending in this application, and stood rejected on various grounds. Claims 58-62 and 66-67 have been canceled, claims 63 and 64 have been amended. All amendments are fully supported by the specification as originally filed, and do not add new matter.

Applicants recently made a photocopy of U.S. Application 09/918,585 filed 7/30/2001, of which the instant application is a continuation, from the PTO's files. All references to page and line numbers made in the foregoing amendments to the specification, and throughout this response are based on the locations in the application photocopied from the PTO files by the Applicants. All amendments in the specification are of formal nature, and do not add new matter.

### *Specification*

The disclosure was objected to because it contained embedded hyperlinks and/or other form of browser-executable code. Applicants have reviewed the application and deleted all references to embedded hyperlinks and/or browser-executable code.

Further, the ATCC address on page 376, line 34, has been updated.

Finally, Applicants amended the title of this application, in order to make this more specific.

The current amendments are believed to obviate all objections to the specification.

### *Double Patenting*

(1) The Examiner notes that a sequence search of the pending and published application databases had revealed that there are a series of applications in which SEQ ID NOS: 369 and 370 are present but that do not claim the polynucleotide. Applicants were requested to point out to the Examiner any double patenting issues.

To the best of their knowledge and after reasonable inquiry, Applicants submit that as of this date they have no other patent applications before the U.S. Patent and Trademark Office that

would contain claims conflicting with claims pending in the present application. This statement is made with candor and good faith under 37 CFR 1.56.

(2) The Examiner found that claims 58-69 of the present application conflict with claims 15-17, 19-27, 29, 30, 31 and 47 of Application No. 09/978,189. Since 09/978,189 is the Serial No. of the present application, the rejection is not understood. Applicants assume that the Examiner bases this rejection on the Publication of one of the parallel applications having the same specification, not taking into account a Preliminary Amendment filed along with the application. Accordingly, the present rejection is likely to be misplaced. Should the Examiner maintain the rejection, she is respectfully requested to properly identify the allegedly conflicting application.

(3) The Examiner found that claims 63-69 are directed to the same invention as that of claims 15-17, 19 and 47 of commonly assigned application Serial No. 09/816,920. Applicants were requested to resolve the issue of priority under 35 U.S.C. 102(g) and possibly 35 U.SC. 102(f) of this single invention. Application Serial No. 09/816,920 has been abandoned, and a continuation application was filed on March 2, 2004 and assigned Serial No. 10/791,618. In Application Serial No. 10/791,618, in a Preliminary Amendment filed on _____, the claims potentially overlapping with claims pending in the present application have been deleted. The present Amendment and Response is accompanied by a Correction of Inventorship under 37 C.F.R. § 1.48(b), deleting all inventors who have not made an inventive contribution to the invention claimed in the present application. Accordingly, there are no issues of priority under 35 U.S.C. 102(f) or (g), and the present rejection should be withdrawn.

(4) Claims 63-69 have been provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 15-17, 19 and 47 of copending Application No. 09/816,920. As discussed above, Application Serial No. 09/816,920 has been abandoned, and its continuation, Application Serial No. 10/791,618 has no claims that would overlap with any of the claims pending in the present application. Accordingly, the present rejection should be withdrawn.

(5) Claims 58-62 have been provisionally rejected under the judicially created doctrine of obviousness type double patenting. The rejection does not identify the copending

application and the claims in the copending application that forms the basis for this rejection. Assuming that the rejection is over application Serial No. 09/816,920, it should be withdrawn in view of the abandonment of that application, and the amendment of its continuation Application Serial No. 10/791,618.

(6) Claim 70 has been provisionally rejected under the judicially created doctrine of obviousness type double patenting over claims 15-17, 19 and 47 of copending application No. 09/816,920 in view of Hopp et al., U.S. Patent No. 5,011,912. The abandonment of application Serial No. 09/816,920 and the amendment of its continuation Application Serial No. 09/816,920 moot this rejection.

***Formal Matters***

Applicants note the acknowledgement of the ATCC deposit of a cDNA clone encoding the PRO273 polypeptide. The foregoing amendment to the specification corrects the address of ATCC, and further elaborates on the conditions of the deposit, which was made for patent purposes, under the terms of the Budapest treaty. Finally, Applicants disagree with the Examiner's assertion that the deposit was necessary for enablement of the current invention. The current invention is fully enabled by the disclosure of the present application, including the sequence of PRO273 and its coding sequence.

***Claim Rejections - 35 USC § 112***

(1) Claims 58-70 have been rejected under 35 U.S.C. 112, second paragraph, as allegedly indefinite in their reference to the extracellular domain of the polypeptide of SEQ ID NO: 370, which is a chemokine and hence a secreted protein. Claims 58-62, and 66-67 have been canceled; claims 63 and 69 have been amended. Since the remaining claims no longer recite an extracellular domain, this rejection is believed to be moot.

(2) Claims 58-62, 69 and 70 have been rejected under 35 U.S.C. 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors were in the possession of the invention at the time the application was filed.

Claims 58-62 have been canceled, and claims 69 and 70 not depend on claim 63, not rejected under this section. Accordingly, the Examiner is respectfully requested to withdraw the present rejection. Applicants note that the Examiner has acknowledged that isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 307, with or without the signal sequence, meet the written description requirement of 35 U.S.C. §112, first paragraph.

***Priority Determination***

The Examiner states that the effective priority date of the instant application is considered to be the filing date of parent application 09/918,585, July 30, 2001, since, according to the Examiner, the utility of stimulating proliferation of mammalian fibroblast cells in culture was first disclosed in that application. Other utilities, such as those based on the mixed lymphocyte reaction (MLR) were not accepted as a specific and substantial asserted utility.

Applicants respectfully disagree and submit that the invention claimed in the present application is entitled to the November 3, 1997 filing date of provisional application Serial No. 60/064249, and the April 27, 1998 filing date of provisional application Serial No. 60/083336.

*Utility - Legal Standard*

According to the Utility Examination Guidelines ("Utility Guidelines"), 66 Fed. Reg. 1092 (2001) an invention complies with the utility requirement of 35 U.S.C. §101, if it has at least one asserted "specific, substantial, and credible utility" or a "well-established utility."

Under the Utility Guidelines, a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the conditions that is to be diagnosed.

The requirement of "substantial utility" defines a "real world" use, and derives from the Supreme Court's holding in *Brenner v. Manson*, 383 U.S. 519, 534 (1966) stating that "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility." In explaining the "substantial utility" standard, M.P.E.P. §2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar

formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather, **any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient**, at least with regard to defining a "'substantial'" utility.'" (M.P.E.P. §2107.01, emphasis added.) Indeed, the Guidelines for Examination of Applications for Compliance With the Utility Requirement, set forth in M.P.E.P, §2107 II (B) (1) gives the following instruction to patent examiners: "If the applicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."

Finally, the Utility Guidelines restate the Patent Office's long established position that any asserted utility has to be "credible." "Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record . . . that is probative of the applicant's assertions." (M.P.E.P. §2107 II (B) (1) (ii)) Such a standard is presumptively satisfied unless the logic underlying the assertion is seriously flawed, or if the facts upon which the assertion is based are inconsistent with the logic underlying the assertion (Revised Interim Utility Guidelines Training Materials, 1999).

The PTO also sets forth the evidentiary standard as to utility rejections. In general, an Applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. §101, "unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope." *In re* Langer, 503 F.2d 1380,1391, 183 USPQ 288, 297 (CCPA 1974). See, also *In re* Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980); *In re* Irons, 340 F.2d 974, 144 USPQ 351 (1965); *In re Sichert*, 566 F.2d 1154, 1159, 196 USPQ 209, 212-13 (CCPA 1977).

Compliance with 35 U.S.C. §101 is a question of fact. *Raytheon v. Roper*, 724 F.2d 951, 956, 220 USPQ 592, 596 (Fed. Cir. 1983) cert. denied, 469 US 835 (1984). The evidentiary standard to be used throughout *ex parte* examination in setting forth a rejection is a preponderance of the totality of the evidence under consideration. *In re* Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). Thus, to overcome the presumption of truth that

an assertion of utility by the applicant enjoys, the Examiner must establish that it is more likely than not that one of ordinary skill in the art would doubt the truth of the statement of utility. Only after the Examiner made a proper *prima facie* showing of lack of utility, shifts the burden of rebuttal to the applicant. The issue will then be decided on the totality of evidence.

*Proper Application of the Legal Standard*

Provisional application Serial No. 60/064249 (copy enclosed) identifies PRO273 as a chemokine having homology to the known macrophage inflammatory protein-2 (MIP-2). According to the last sentence of Example 1: *"Analysis of the amino acid sequence of the full-length PRO273 polypeptide suggests that portions of it possess significant homology to the human macrophage inflammatory protein-2 as shown in Figures 5-19, thereby indicating that PRO273 may be a novel chemokine."*

The application further describes that MIP-2 is a member of the C-X-C family of chemokines, which is chemotactic for human neutrophils and induces local neutrophil infiltration when injected into the foot pads of mice. The disclosure goes on stating that MIP-2 is chemotactic for rat neutrophils but does not stimulate migration of rat alveolar macrophages or human periperal blood eosinophils or lymphocytes, and that rat MIP-2 has been shown to stimulate proliferation of rat alveolar epithelial cells but not fibroblasts.

In the second to last paragraph of the "BACKGROUND OF THE INVENTION" section, the provisional application states: *"Current techniques for diagnosis of abnormalities in inflamed or diseased issues mainly rely on observation of clinical symptoms or serological analyses of body tissues or fluids for hormones, polypeptides or various metabolites. Problems exist with these diagnostic techniques. First, patients may not manifest clinical symptoms at early stages of disease. Second, serological tests do not always differentiate between invasive diseases and genetic syndromes. Thus, the identification of expressed chemokines is important to the development of new diagnostic techniques, effective therapies, and to aid in the understanding of molecular pathogenesis."*

The "BACKGROUND OF THE INVENTION" section of the second provisional application, Serial No. 60/083336 additionally states: *"To date, chemokines have been*

*implicated in at least the following conditions: psoriasis, inflammatory bowel disease, renal disease, arthritis, immune-mediated alopecia, stroke, encephalitis, MS, hepatitis, and others. In addition, non-ELR-containing chemokines have been implicated in the inhibition of angiogenesis, thus indicating that these chemokines have a rule in tumor vascularization and tumorigenesis. Therefore it is the object of this invention to identify polypeptides and nucleic acids encoding the same which have sequence identity and similarity with cytokine-induced neutrophil chemoattractants, MIP-1, MIP-2, and other related proteins. The efforts of this object are provided herein."*

Indeed, in 1997 MIP-2 was known to play a role in lung neutrophil influx after heptic ischemia/reperfusion injury (Carrick et al., J. Surg. Res. 68(1):16-23 (1997) - copy enclosed). It was also proposed that MIP-2 plays a role in neutrophil infiltration in allergic inflammation (Xiao et al., Biochem. Biophys. Acta 1361(2):138-146 (1997)). Subsequent evidence also supports the utilities asserted in the two provisional applications, the priority of which is claimed. For example, Cao et al., J. Immunol. 165:2588-2595 (2000) (cited in the Office Action) experimentally confirms the involvement of a highly homologous protein, designated MIP-2γ in neutrophil trafficking.

Based on this disclosure, at the November 3, 1997 filing date of provisional application Serial No. 60/064249, or at least at the April 27, 1998 filing date of provisional application Serial No. 60/083336, one skilled in the art would have understood that PRO273 is an inflammatory chemokine, which finds utility in the diagnosis and treatment of inflammatory diseases which benefit from the recruitment of neutrophils to the site of inflammation, and is a target for identifying and developing drugs to treat diseases where neutrophil influx is part of the pathology.

In conclusion, Applicants request that November 3, 1997, or at least April 27, 1998 should be accorded as priority to all claims pending in this application.

***Rejections over Prior Art***

(1) Claims 58-70 have been rejected under 35 U.S.C. 102(b) as anticipated by Chen et al., WO 99/33990, July 8, 1999. According to the rejection, Chen et al. disclose a nucleic acid

(SEQ ID NO: 1) that is 100% identical to nucleotides 167-502 of SEQ ID NO: 369 of the instant application (ORF between nucleotides 167 and 499), and encodes a polypeptide (Tim-1 CXC chemokine; SEQ ID NO: 2), that is 100% identical to the PRO273 polypeptide of SEQ ID NO: 370 of the present application.

As discussed earlier, all claims currently pending are entitled to the November 3, 1997 filing date of provisional application Serial No. 60/064249, and to the April 27, 1998 filing date of provisional application Serial No. 60/083336, each of which precedes the effective date of Chen et al. Accordingly, Chen et al. is not prior art, and the present rejection should be withdrawn.

(2) Claims 58-62, 69 and 70 have been rejected under 35 U.S.C. 102(e) as anticipated by Ni et al., U.S. Patent No. 5,910,431, which claims the priority of March 19, 1996. Ni et al. discloses nucleic acid encoding a polypeptide that is 99.1% identical to the PRO273 polypeptide of SEQ ID NO: 370 of the present application.

The cancellation of claims 58-62 obviates their rejection. Claims 69 and 70 now depend from Claim 63, which is not rejected under this section. Accordingly, the present rejection should be withdrawn.

(3) Claims 58-62, 69 and 70 have been rejected under 35 U.S.C. 102(a) as anticipated by Cao et al., J. Immunol. 165:2588-2595 (September 2000). Claims 58-62 have been canceled, which moots their rejection. Claims 69 and 70 now depend from Claim 63, which is not rejected under this section, accordingly, their rejection should be withdrawn. In addition, Applicants note that all claims pending in this application are entitled to the November 3, 1997 filing date of provisional application Serial No. 60/064249, and to the April 27, 1998 filing date of provisional application Serial No. 60/083336. Therefore, Cao et al. is not a valid reference.

(4) Claims 63-69 were rejected under 35 U.S.C. 102(f) "because the applicant did not invent the claimed subject matter." In support of the rejection, the Examiner refers to commonly assigned Application Serial No. 09/816,920, which names Sherman Fong, Audrey Goddard, Kenneth Hillan, Iris Roth and William Wood as inventors.

A Correction of Inventorship under 37 C.F.R. § 1.48(b) is filed concurrently herewith, leaving Sherman Fong, Audrey Goddard, Kenneth Hillan and William Wood as inventors in the present application. Iris Roth did not make any inventive contribution to the invention currently claimed, and therefore has not been named as an inventor. Application Serial No. 09/816,920 has been abandoned, and a continuation application was filed on March 2, 2004 and assigned Serial No. 10/791,618. Since the inventions currently claimed in the present application and in Application Serial No. 10/791,618 are different, any difference between the inventive entities in the two applications should not raise any issues under 35 U.S.C. 102(f) or 102(g).

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited. Should there be any further issues outstanding, the Examiner is invited to contact the undersigned attorney at the telephone number shown below.

Please charge any additional fees, including fees for additional extension of time, or credit overpayment to Deposit Account No. **08-1641** (referencing Attorney's Docket No. **39780-2630 P1C7**).

Respectfully submitted,

Date: October 21, 2004

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